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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/069,923	05/10/2002	Des Richardson	1871-134	9609

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EXAMINER	
ROBINSON, BINTA M	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/069,923	RICHARDSON ET AL.	
	Examiner	Art Unit	
	Binta M Robinson	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-6 and 8-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1,2 and 4* is/are allowed.

6)☒ Claim(s) *5,6 and 8-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/27/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

The 112, first paragraph, rejection of claims 1-10, 15, and the 102 (b) rejections of claims 1-5 over Schurter, the 102 (b) rejection of claims 1-7 and 9 over Schurter and Schwamborn made at paper no. 8 are withdfrawn in light of applicant's comments and amendments. In response to the applicant's arguments that the claims are not drawn to iron overload diseases per se, the examiner notes that claim 11 is drawn to treating iron overload diseases per se, and that the specification has not enabled the treatment of all iron overload diseases. It has been established in the art that iron chelators do not treat Friedreich's ataxia and B-thalassemia with great efficacy. 2-pyridylcarboxaldehyde isonicotinoyl hydrazone analogs do not have beneficial effects on Friedreich's ataxia (FA) patients. (See Richards, Expert Opinion on Investigational Drugs, Reference U). The drug, desferrioxamine as an iron chelator has been found to not be an effective treatment for thalassemia. The use of low-Mr Fe chelators for the treatment of B-thalassaemia and FA is challenging owing to the potential of these compounds to cause toxicity. (See Richardson, American J. of Hematology, 73: 200-210 (2003). It is not established in the art to treat iron overload diseases other than B-thalassemia and Friedreich's ataxia with iron chelators.

(Modified rejection)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5, 6, 8, 9, 10-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement for all iron overload diseases, including Friedreich's ataxia and B-thalassemia. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The specification does disclose pharmacological data on the chelation activity of these compounds in in vitro experiments. However, the specification does not give any guidance as to whether or not this in vitro data correlates to in vivo settings, particularly in terms of treating the diseases claimed.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The Nature of the Invention

The nature of the invention in claims 5, 6, 8, 9, 10-14 is the treatment of iron overload diseases with a compound of claim 1.

The State of the Prior Art

The state of the prior art is that that lower or higher concentrations of iron in the body can be fatal if timely precautions are not undertaken. Transfusional iron-overload

is one such type of problem, which has affected tens of thousands of patients all over the world. 2-pyridylcarboxaldehyde isonicotinoyl hydrazone analogs do not have beneficial effects on Friedreich's ataxia (FA) patients. (See Richards, Expert Opinion on Investigational Drugs, Reference U). The drug, desferrioxamine as an iron chelator has been found to not be an effective treatment for thalassemia. The use of low-Mr Fe chelators for the treatment of B-thalassaemia and FA is challenging owing to the potential of these compounds to cause toxicity. (See Richardson, American J. of Hematology, 73: 200-210 (2003).

The predictability or lack thereof in the art

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to therapeutic effects of iron-mediated diseases, whether the iron was chelated or not would affect the possible treatment of any disease.

Hence, in the absence of a showing of correlation between all the diseases claimed as capable of treatment by the compound of claim 1 and the chelation of iron, one of skill in the art is unable to fully predict possible results from the administration of the compound of claim 1 due to the unpredictability of the role of iron.

The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The amount of direction or guidance present

The direction present in the instant specification is that the compounds of claim 1 can chelate iron. The specification does disclose pharmacological data on the chelation activity of these compounds in in vitro experiments. However, the specification does not give any guidance as to whether or not this in vitro data correlates to in vivo settings, particularly in terms of treating the diseases claimed.

The presence or absence of working examples

There are no working examples for any diseases listed in the specification. The specification does disclose pharmacological data on the chelation activity of these compounds in in vitro experiments. However, the specification does not give any guidance as to whether or not this in vitro data correlates to in vivo settings, particularly in terms of treating the diseases claimed.

The breadth of the claims

The breadth of the claims is that the compound of claim 1 can treat any iron overload disease.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what listed diseases would be benefited by the chelation of iron and would furthermore then have to determine whether the claimed compounds would provide treatment of the all iron overload diseases.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of the claim 1 for the treatment of any iron overload disease. As a result necessitating one of skill to perform an exhaustive search for which iron overloaded diseases can be treated by the compound of claim 1 in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search , but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling

disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which iron overloaded diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

Claims 1, 2, 4 are allowable.

The IDS filed 7/27/04 has been considered.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (571) 272-0692. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562.

A facsimile center has been established. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machine are (703)308-4242, (703)305-3592, and (703)305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)-272-1600.

Cecilia Tsang

Cecilia J. Tsang
Supervisory Patent Examiner
Technology Center 1600

BMR
September 17, 2004